Vulnerable Plaque Characterization Using Temporal and Spatial Speckle Analysis

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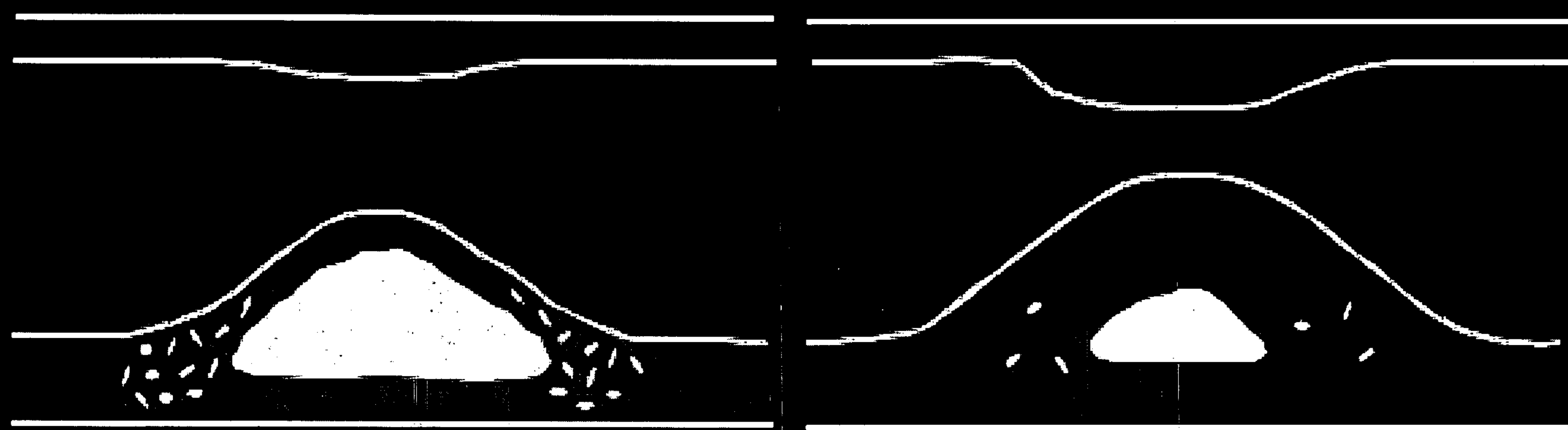
Vulnerable Plaques

Vulnerable Plaque | Stable Plaque



Vulnerable Plaque		Stable Plaque
Thin	**Cap**	Thick
Abundant	**Macrophages**	Few
High	**Lipid Conc.**	Low

Vulnerable Plaque Diagnosis

Proposed Diagnostics

- Infrared
  - **Indirectly measures lipid content of plaque**
- Fluorescence
  - **Measures autofluorescence**
    - **Collagen**
    - **MMP**
- IVUS
  - **Structural measurement of cap**
  - **Poor resolution**
- OCT
  - **Structural measurement of cap**
  - **Sufficient resolution for measurement of cap thickness**

Proposed methods do not measure the biomechanical properties of plaque

Intrinsic Plaque Biomechanics

Biomechanical properties

- Cap strength
  - Proportional to thickness and structural integrity
- Lipid pool
  - Shear stress and strain on cap are related to lipid pool stiffness
  - Rupture of plaque tends to occur in areas of large stiffness gradient between cap and lipid pool
  - Lipid lowering drugs increase stiffness of lipid pool
  - Stiffening of the lipid pool decreases vulnerability

Mechanical stiffness of the cap and lipid pool are essential parameters for assessing the likelihood of plaque rupture

Viscosity

Viscosity of tissue is proportional to stiffness

- Related to the ability of the molecules in the tissue matrix to move

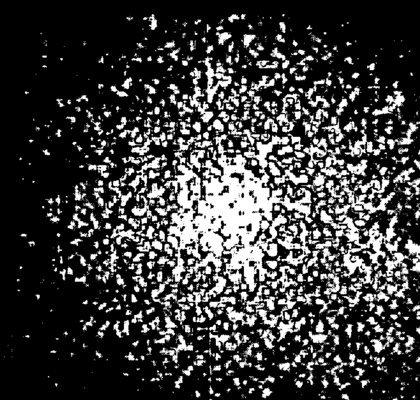
Brownian motion

- Random motion of particles in the matrix
- Brownian motion is inversely proportional to viscosity and stiffness
  - **Low stiffness, rapid Brownian motion**
  - **High stiffness, slow Brownian motion**

Brownian motion velocity is a measurement of tissue stiffness

Speckle

Coherent interference of light remitted from a scattering media or substrate



- Produces a grainy pattern at the surface of the specimen and in the image plane
- The pattern is created from the remitted field after many multiple scattering events within the specimen
- Motion of a single scatterer in the specimen changes the speckle pattern

Speckle Motion

Motion of a single scatterer in the specimen changes the speckle pattern

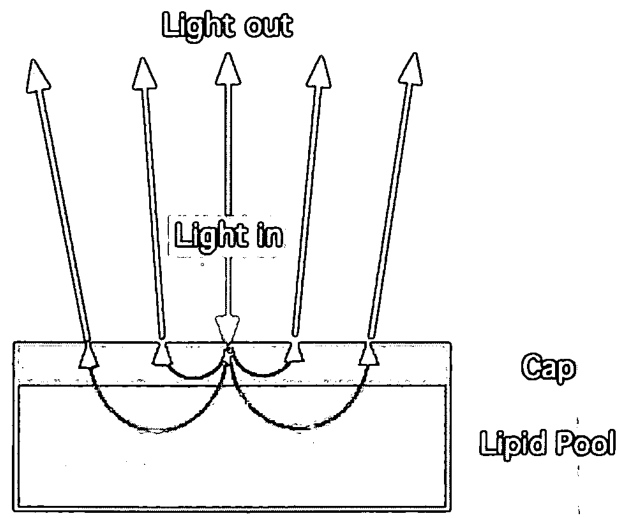
- The time dependent speckle pattern can be used to determine the Brownian motion within a multiply scattering media
- The motion is characterized by the spatial decorrelation of the speckle pattern as a function of time
- For Brownian motion, the decorrelation is a negative exponential with a time constant, τ

Stiffness of the cap and lipid pool can be determined by measuring the speckle decorrelation time constant

Light Diffusion

In tissue, light remitted further from the beam entry point has probed deeper into the tissue

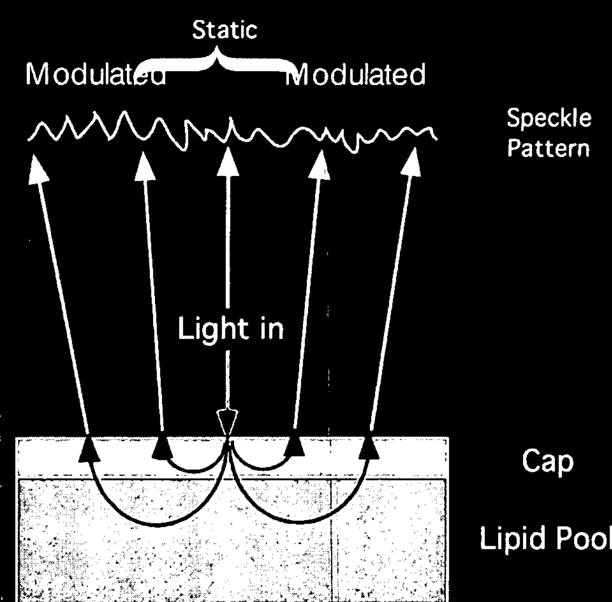
- Governed by the optical properties of tissue



Spatial and Temporal Characterization of Plaques

Measuring the speckle decorrelation time, τ, as a function of distance from beam entry point allows measurement of Brownian Motion and

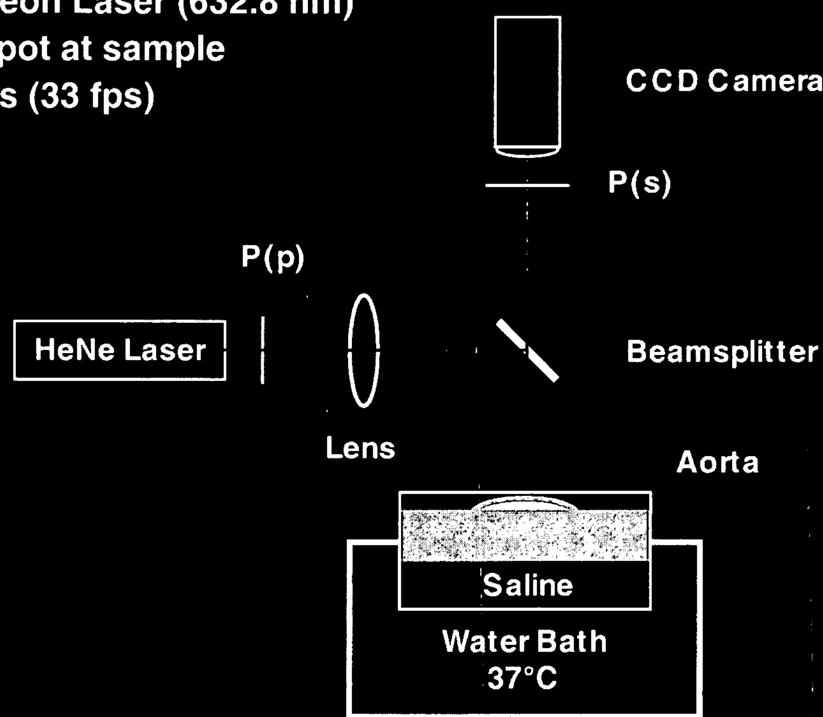
- Cap thickness
- Cap stiffness
- Lipid pool stiffness

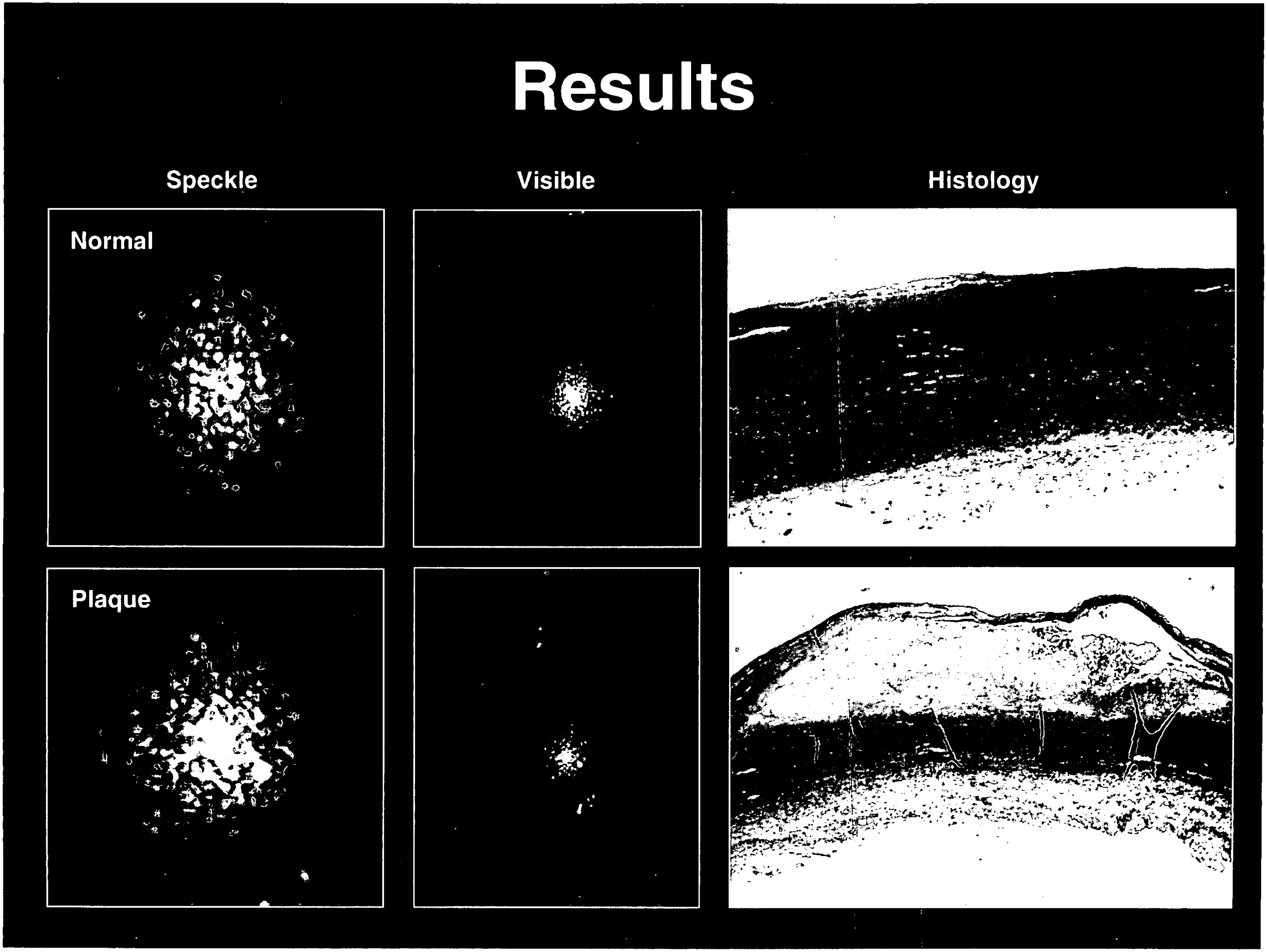


Proof of Principle

Methods

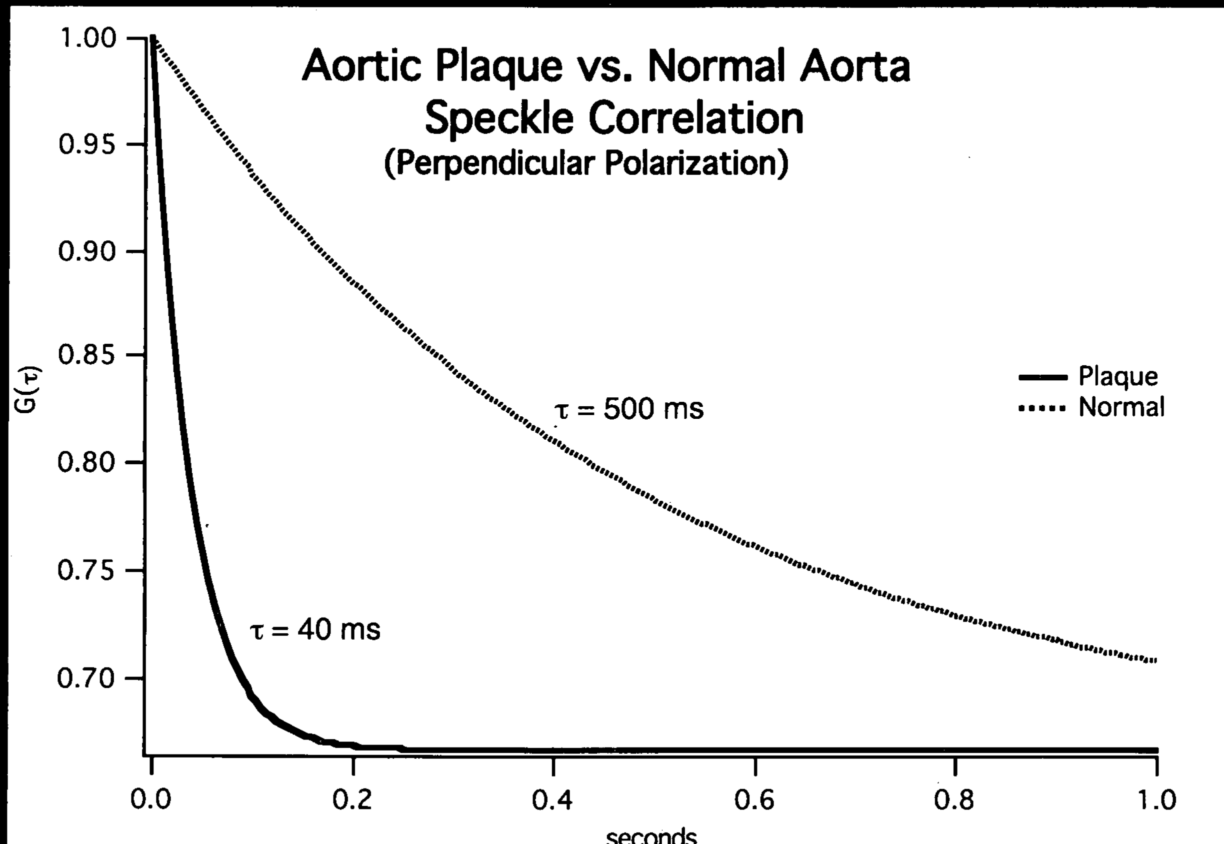
- Cadaveric aortas
- Normal saline, 37°C
- Helium Neon Laser (632.8 nm)
- 100 μm spot at sample
- 2 seconds (33 fps)





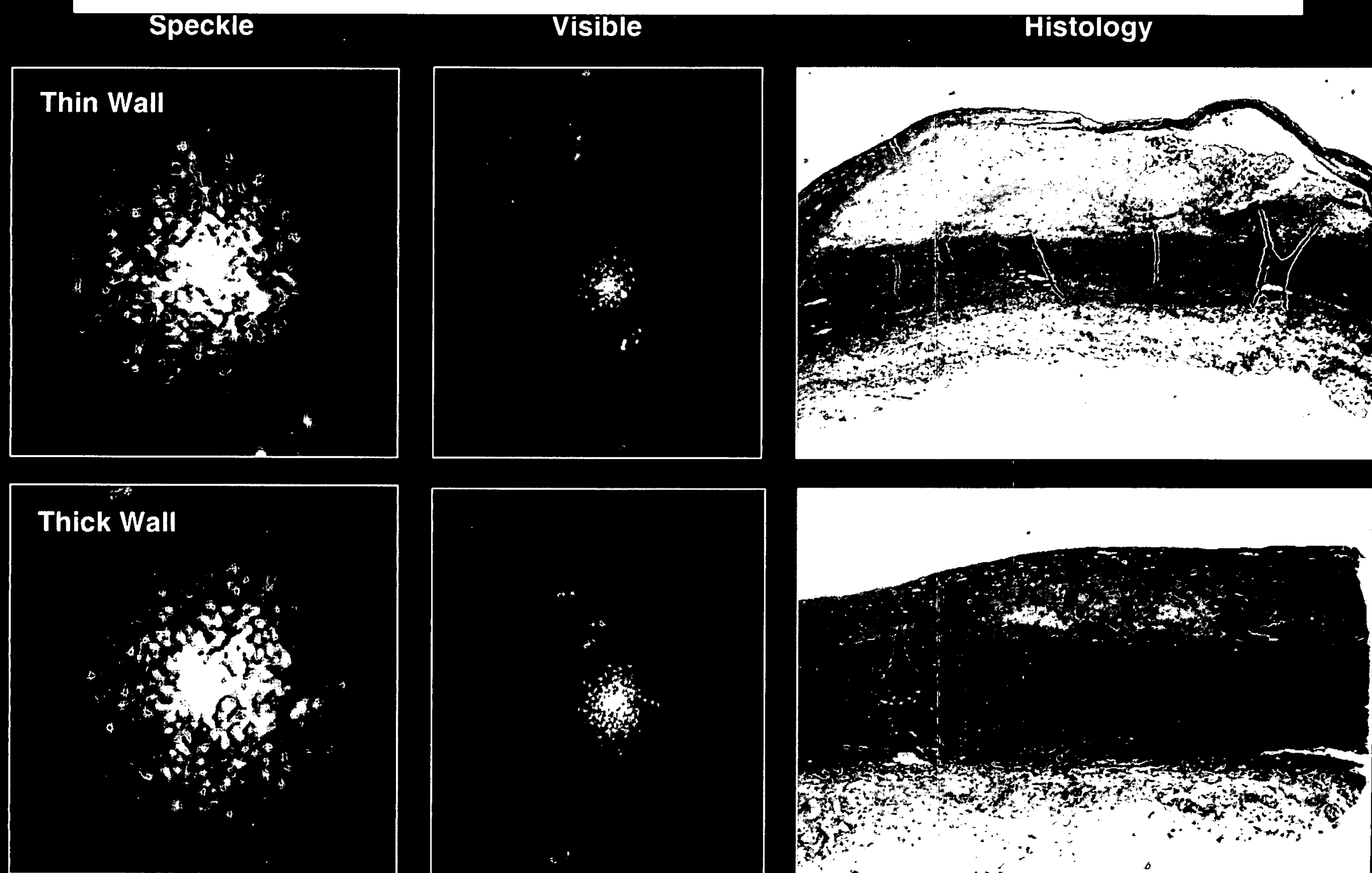
Results
Speckle
Visible
Histology
Normal
Plaque

Results



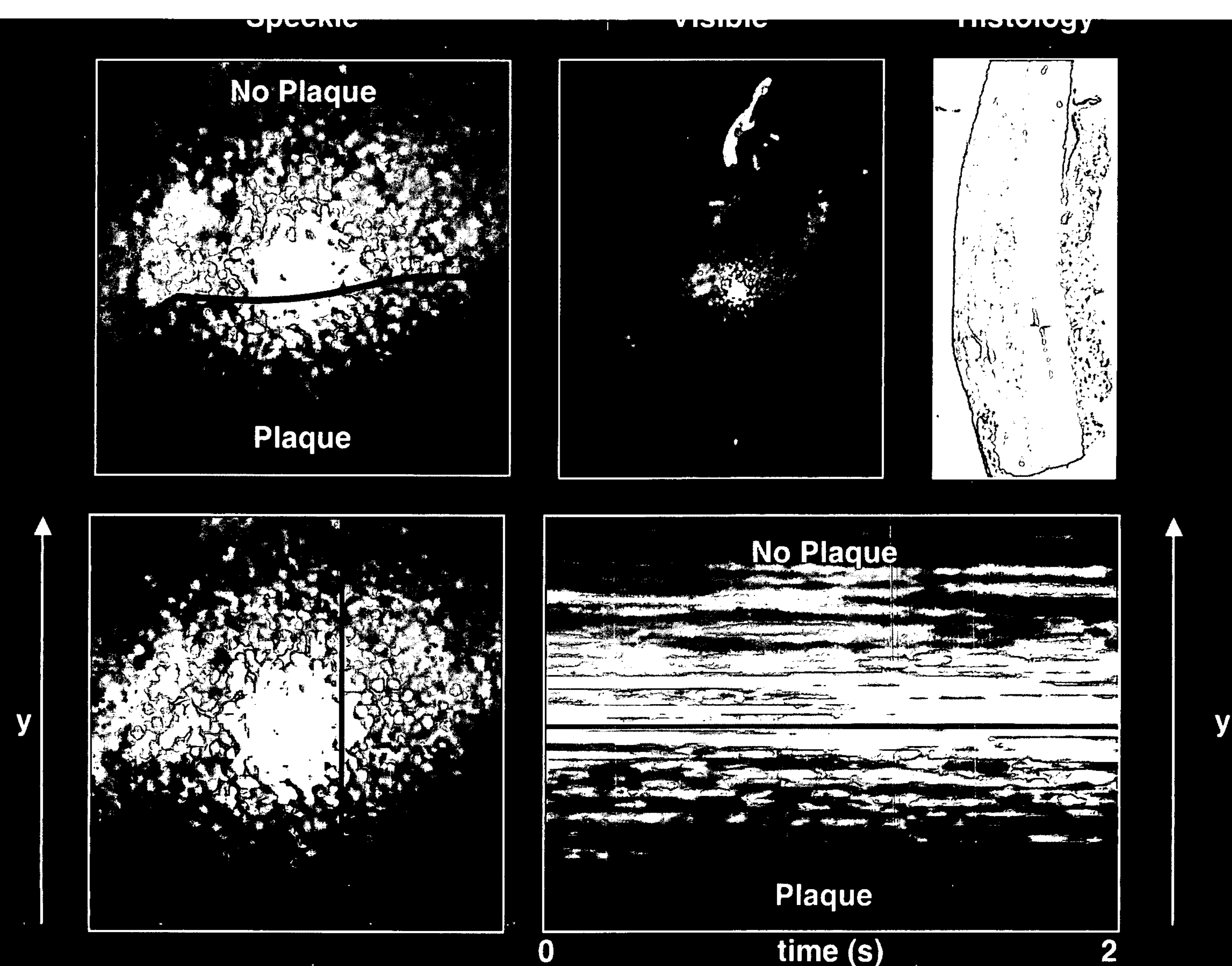
Aortic Plaque vs. Normal Aorta
Speckle Correlation
(Perpendicular Polarization)
G(τ)
1.00
0.95
0.90
0.85
0.80
0.75
0.70
0.0
0.2
0.4
0.6
0.8
1.0
seconds
τ = 500 ms
τ = 40 ms
Plaque
Normal

Results
(Aortic Plaques)



Results

(Spatial Localization)



Feasibility Study Summary

Speckle decorrelation time constant is different between normal aorta and plaque

- τ = 500 ms vs 40 ms

Speckle decorrelation time constant is different between thin and thick-walled plaques

- Greater for thick-walled plaques

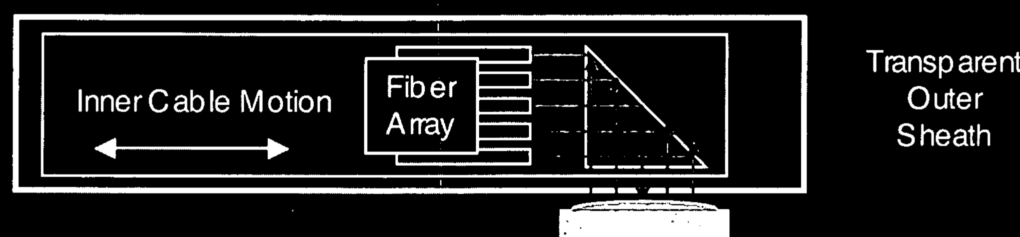
Speckle decorrelation is spatially dependent

- Border between plaque and normal aorta demarcates different speckle decorrelation time constants

Clinical Realization

Catheter based technique **(one possibility)**

- Array of fibers
- Scanned probe



Difficulties

- Intrinsic heart and catheter motion
  - **Lipid pool Brownian motion time constant is approximately 40 ms**
- Blood
  - **Will need saline infusion and/or direct contact with tissue**

Alternative Methods
(Spatial Localization)

Localize time and space (x, y, z) dependent speckle patterns using optical methods as opposed to light diffusion

- Confocal microscopy
  - Apertures in the source and detector planes combined with a high numerical aperture imaging lens
  - High resolution speckle analysis in (x, y, z)
  - Speckle decorrelation is less sensitive than multiple scattering technique
- Optical Coherence Tomography (OCT)
  - Uses low coherence interferometry to obtain localization in z
  - Measures cap thickness directly
  - Speckle decorrelation is less sensitive than multiple scattering technique

Conclusion

Temporal and spatial analysis of the speckle patterns can potentially determine

- Cap thickness
- Cap and plaque viscosity
- Spatially resolved biomechanical stiffness
- <u>Plaque vulnerability</u>

Future work

- Speckle statistics
  - **Can determine cap thickness and optical properties**
  - **Low coherence light**
- Strain and stress measurements
  - **Correlate biomechanical properties with Brownian motion measured by speckle decorrelation**
- Probe development
- Continue cadaveric aorta studies
- In vivo studies (e.g. rabbit model)